REMARKS/ARGUMENTS

Upon entry of this Amendment, Claims 13, 14, 18, 19 and 21-25 will be pending in the application. Claims 1-12 and 26-32 have been canceled with the understanding that the subject matter thereof may subsequently be presented in the form of a continuation application.

The undersigned would like to thank Examiner Kishore for the courtesies extended during the telephone interview conducted July 27, 2004.

As proposed during the interview, independent Claim 13 has been amended to recite a method for treating sexual dysfunction in a female patient comprising topically administering to the genitals of said patient an effective amount of esterified L-arginine comprising ethyl ester of L-arginine and an effective amount of an antioxidant. Basis for the language of amended Claim 13 is provided in the specification, for example, at page 4, line 26, page 5, line 17, and originally filed Claims 16 and 17. Claims 15, 16, 17 and 20, which originally depended from Claim 13, have been canceled.

As discussed during the interview, Applicants have unexpectedly found that topically applied compositions comprising ethyl ester of L-arginine are highly effective in treating female sexual dysfunction, particularly in comparison with similar compositions containing L-arginine. The presently claimed invention thus provides unexpectedly improved results in comparison with prior art compositions and methods. A Rule 132 Declaration of Meir S. Sacks is submitted herewith in support of Applicants' position that the present invention provides unexpectedly improved results.

35 U.S.C. § 112 Rejection

Claims 1-12 were rejected under 35 U.S.C. § 112, first paragraph, due to an alleged lack of enablement for the terms "L-arginine derivatives" and "antioxidants". By the present Amendment, the term "L-arginine derivative" has been removed from Claim 13, and the claim now recites an "esterified L-arginine comprising ethyl ester of L-arginine". It is submitted that Claim 13, as amended, fully meets the enablement requirement of 35 U.S.C. § 112, first paragraph. It is noted that the examples beginning at page 9 of the specification describe actual studies performed on women involving

topical application of compositions comprising the ethyl ester of L-arginine and an antioxidant comprising ascorbic acid. The specification therefore provides an adequate description to those skilled in the art how to make and use the claimed invention.

35 U.S.C. § 103(a) Rejections

Independent Claim 13 was rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,207,713 to Fossel or U.S. Patent No. 6,476,037 to Wallace in view of U.S. Patent No. 6,139,847 to Chobanian et al. The Office Action states that:

> The inclusion of an antioxidant in the L-arginine containing compositions of Fossel or Wallace for the treatment of erectile dysfunction would have been obvious to one of ordinary skill in the art, with the expectation of obtaining at least an additive effect, since Chobanian teaches that antioxidants are NO catabolism inhibitors and that they could be used in combination with NO stimulators. Although neither Fossel nor Wallace teach the use of the composition for female sexual dysfunction by topical application to the clitoris, it would have been obvious to one of ordinary skill in the art to use the composition for females with a reasonable expectation of success since the clitoris is supplied with blood vessels and the principle of vasodilatation is the same.

Independent Claim 13 was further rejected under 35 U.S.C. § 103(a) as being unpatentable over the Fossel '713, Wallace '037 and Chobanian et al. '847 patents in view of U.S. Patent No. 6,007,824 to Duckett et al. by itself or in further combination with U.S. Patent No. 6,031,002 to Wysor. The Office Action states that:

> Duckett et al as discussed before, disclose compositions containing L-arginine and ginseng (antioxidant) for the treatment female sexual dysfunction. Duckett et al teach that the sexual stimulation causes local release of NO resulting in the smooth muscle relaxation and the increased blood flow. They further teach that L-arginine releases NO resulting in smooth muscle relaxation and increased inflow of blood (note the abstract, col. 1, line 12 through col. 2, line 46, col. 3, line 65 through col. 4, line 50 and claims). The mode of administration in Duckett however, is oral and not topical.

> Wysor as discussed before, while disclosing prostaglandin (vasodilator) formulations for enhancing female sexual response teaches that the formulations can be applied topically to the genitals and such a topical treatment is highly effective. Wysor further teaches the use of liposome formulations for the delivery of the composition (note the abstract, columns 1-3 and claims).
>
> In essence, the reference of Duckett shows that the principle of NO release and the increased blood flow in females by the vasodilator, arginine and that of Wysor shows that a vasodilator can be applied topically the genitals to treat female sexual dysfunction.
>
> One of ordinary skill in the art would be motivated further to use the composition of arginine and the antioxidants of Fossel, Wallace and Chobanian to treat the female dysfunction since the effectiveness of arginine against female dysfunction and that of Wysor shows that a vasodilator composition can be applied topically to the female genitals to achieve the desired goal.

It is submitted that Claim 13, as amended, distinguishes over the prior art of record. As discussed in detail during the interview, none of the applied references alone, or in combination, disclose a method for treating sexual dysfunction in a female patient in which an effective amount of esterified L-arginine comprising ethyl ester of L-arginine and an effective amount of an antioxidant are topically administered to the genitals of the female patient. The Fossel et al. '713 patent discloses oral administration of L-arginine to produce enhanced blood flow in tissue which is said to cause beneficial effects such as warming cold tissue of the hands and feet, promoting hair growth, overcoming male erectile failure, etc. Wallace '037 discloses oral administration of L-arginine for the treatment of cardiac pathologies and/or the treatment of erectile dysfunction. Chobanian et al. '847 discloses the combination of angiotensin inhibitors and nitric oxide stimulators to slow and reverse the process of fibrosis in the body. Duckett et al. '824 discloses the treatment of sexual dysfunction using a combination of L-arginine, ginseng and Zizyphi fructose in an orally administered dosage. Wysor '002 discloses the enhancement of female sexual response by topical administration of a prostaglandin vasodilator.

Even if the foregoing references could properly be combined as proposed in the Office Action, such a combination fails to render the presently claimed invention obvious. The prior art of record does not teach or suggest topical administration to the genitals of a female patient an effective amount of esterified L-arginine comprising ethyl ester of L-arginine and an effective amount of an antioxidant.

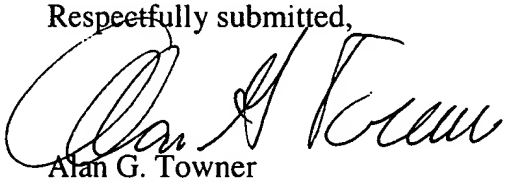
Moreover, the prior art of record fails to recognize the unexpectedly improved results achieved in accordance with the presently claimed invention. Applicants have surprisingly and unexpectedly found that compositions comprising esterified L-arginine comprising ethyl ester of L-arginine and an antioxidant significantly enhance sexual response in females when topically applied.

In support of Applicants' position that the presently claimed method provides unexpectedly improved results, a Rule 132 Declaration of Meir S. Sacks is submitted herewith. The Sacks Declaration demonstrates that a composition of the presently claimed invention comprising ethyl ester of L-arginine produces unexpectedly improved results when applied to the genitals of female subjects in comparison with a composition comprising no active ingredient. The Sacks Declaration further demonstrates that a composition of the presently claimed invention comprising ethyl ester of L-arginine produces unexpectedly improved results when applied to the genitals of female subjects in comparison with a similar composition comprising L-arginine instead of the ethyl ester of L-arginine. As described in detail in the Sacks Declaration, application of a composition to the genitals of female subjects in accordance with the present invention resulted in significantly enhanced sexual responses. In view of the unexpectedly improved results achieved in accordance with the presently claimed method, it is submitted that the presently claimed invention as recited in Claim 13 is patentable over the prior art of record.

In view of the foregoing amendments and remarks, and the accompanying Sacks Declaration, it is submitted that Claims 13, 14, 18, 19 and 21-25 are patentable over the prior art of record. Accordingly, an early notice of allowance of this application is respectfully requested.

In the event that any outstanding matters remain in connection with this application, the Examiner is invited to telephone the undersigned at (412) 263-4340 to discuss such matters.

Respectfully submitted,



Alan G. Towner
Registration No. 32,949
Pietragallo, Bosick & Gordon
One Oxford Centre, 38th Floor
301 Grant Street
Pittsburgh, PA 15219
(412) 263-4340 Attorney for Applicants